INTRAPULMONARY RECEPTORS IN THE BULLFROG: SENSITIVITY TO CO_2

by

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INTRODUCTION

Recent investigations on a variety of vertebrate animals point to the importance of intrapulmonary CO_2 concentration in the control of breathing (Guz, et al., 1966; Bartoli, et al., 1974; Gatz, et al., 1975; Osborne and Mitchell, 1977). Receptors capable of sensing intrapulmonary CO_2 concentration have been reported in the lungs of birds, reptiles, and mammals. These receptors are of two kinds: (1) intrapulmonary chemoreceptors, whose adequate stimulus is CO_2, present in birds (Fedde et al., 1974; Burger, et al., 1974) and reptiles (Fedde et al., 1977); (2) intrapulmonary mechanoreceptors, whose adequate stimulus is stretch but whose discharge frequency is modulated by CO_2, present in mammals (Mustafa and Purves, 1972; Schoener and Frankel, 1972; Sant'Ambrogio, et al., 1974; Kunz, et al., 1976). This study was designed to determine if the bullfrog, representing Amphibia, also possesses either or both of these receptors.

METHODS

Animals

Fifteen bullfrogs (Rana catesbeiana) ranging from 180g to 550g (average 310g) were used in this study. The animals were collected locally in June and July.

Animal Preparation

Figure 1 shows a diagram of the experimental arrangement and the variables recorded. The frogs were either anesthetized with an intraperitoneal injection of Na phenobarbital (150-170 mg/kg) approximately 12 hours before surgery or were decerebrated under hypothermal anesthesia (1-2° C) in an ice bath. The latter procedure provided the most stable preparation. In both cases, it was necessary to maintain the animals at 1-2° C during

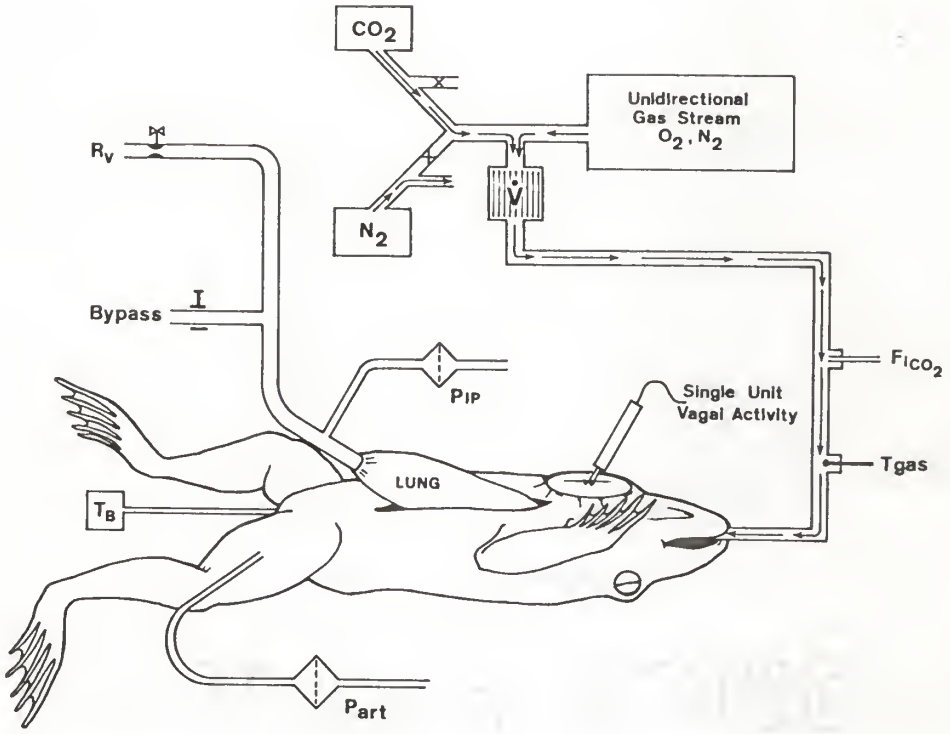

Figure 1. Schematic diagram of the experimental arrangement. Unidirectional ventilation of the left exposed lung allowed independent control of chemical and mechanical stimuli to intrapulmonary receptors. O_2, N_2, and CO_2 were derived from gas cylinders and metered with differential pressure flowmeters. Reduction of CO_2 was accompanied by addition of N_2 to prevent the total flow ($\dot{V}$) (as measured with a pneumotachograph) from changing. F_ICO_2, fractional inspired CO_2; T_{gas}, temperature of gas entering tracheal cannula; T_B, body temperature; P_{art}, arterial blood pressure; P_{ip}, intrapulmonary pressure; R_v, variable resistance valve.

surgery to prevent reflex muscular activity. After surgery, the animals were allowed to warm to room temperature.

A sciatic artery was cannulated to monitor arterial blood pressure. A tracheal cannula, consisting of a glass tube 10 cm long and 0.5 cm diameter, was sutured into the glottis and sealed in place with tissue cement. The animal was then placed on its back, and a longitudinal incision was made in the lateral wall of the abdomen. The left lung was lifted through this opening while the rest of the viscera remained intact. Gauze sponges soaked in frog heart Ringer solution were wrapped around the exposed lung and over the abdominal opening to prevent the viscera from drying. The Ringer solution had the following composition (mM): NaCl, 111; KCl, 1.9; $CaCl_2$ (anhydrous), 1.1; $NaHCO_3$, 2.4; NaH_2PO_4 (anhydrous), 0.08; glucose, 11.1 (Dawson, 1969). A small incision was then made in the apex of the lung, and a short piece of plastic tubing (1 cm OD) was inserted and tied in place. This allowed the animal to be ventilated with a unidirectional stream of gas.

A ventral incision was made in the cervical region, and the vagus nerve was isolated, cut centrally, and placed on a small mirror dissecting platform. The skin surrounding the incision was lifted and sutured to a metal ring to provide a mineral oil pool for dissecting the nerve. To prevent reflex muscular activity during the experiment, succinylcholine (Squibb; initial dose 2 mg) was administered as needed via the arterial cannula, and both sciatic nerves were cut. Body temperature was monitored during the experiment by a telethermometer probe (Yellow Springs Inst. Co.) placed 3-5 cm into the rectum. Body temperature was allowed to fluctuate with room temperature and ranged from 22° C to 27° C.

Ventilation Procedure

A gas mixture of 40% O_2-60% N_2 was used for unidirectional ventilation. The gas was bubbled through warm water for humidification and then passed through a pneumotachograph (Statham-Godart 17212) to measure the flow. Carbon dioxide could be added to or removed from the ventilating gas stream by a magnetic valve system (Fedde, et al., 1974). When CO_2 was removed from the gas, a like amount of N_2 was added to keep the total flow constant at 1.0 $L \cdot min^{-1}$.

A variable resistance valve (R_v) and a bypass tube were mounted in parallel in the gas stream exiting from the lung (fig. 1). The bypass tube could be opened or closed with a pinch clamp, and R_v could be adjusted to maintain a given intrapulmonary pressure (P_{ip}). When the bypass tube was closed, the lung inflated to and maintained the P_{ip} which had been preset with R_v. When the bypass tube was opened, resistance in the gas line was decreased and P_{ip} immediately fell to near 0 cmH_2O. This system allowed rapid inflation and deflation of the lung when testing for mechanosensitivity of receptors.

Recordings

(1) P_{ip}. The P_{ip} was measured with a sensitive pressure transducer (Statham P23BB) connected to the gas line immediately caudal to the lung. The transducer signal was recorded on one channel of an FM tape recorder (Hewlett-Packard 3960) and multi-channel pen recorder (Brush 481).

(2) F_ICO_2. The fractional concentration of CO_2 (F_ICO_2) in the ventilating gas was monitored with an infrared CO_2 analyzer (Beckman, LB-2). Output from the CO_2 analyzer was also recorded on the tape and pen recorders.

(3) Neural recordings. Small filaments of the vagus nerve were dissected free and placed on bipolar tungsten electrodes (μm diameter) to record single-unit afferent activity. The signal was amplified with a

differential amplifier (Grass, P511) and then displayed on one channel of a multi-channel oscilloscope (Tektronix 565). The multiplex output from an amplitude analyzer (Frederick Haer & Co.) was displayed on another channel of the oscilloscope and allowed selective triggering on a single unit. A window pulse output from the amplitude analyzer provided input for a frequency analyzer (Fedde, et al., 1974) which in turn provided an integrated signal of the discharge frequency and a normalized pulse. The integrated frequency signal was recorded only on the pen recorder; the normalized pulse was simultaneously recorded on both pen and tape recorders.

Experimental Procedure

Two procedures were used to search for afferent activity from intrapulmonary receptors when each small neural strand had been placed on the electrode: (1) By momentarily blocking the output of the gas line and raising P_{ip}, activity from stretch-sensitive receptors could be detected. (2) With P_{ip} maintained at 1.0 cmH_2O, F_ICO_2 was continuously cycled from 0 to 0.04 at 0.05 Hz. Thus, CO_2 sensitivity of any receptor whose afferent fiber was in the strand could be detected by its response to the cycling CO_2 concentration.

A series of 3 tests was performed on each unit to quantify the CO_2 sensitivity of the receptor and to determine if the degree of inflation influenced CO_2 sensitivity. These tests were performed as follows: (1) The discharge of the receptor was measured at low P_{ip} when F_ICO_2 was changed from 0 to 0.04 for 5 to 10 cycles at 0.01 Hz; (2) Test 1 was repeated with F_ICO_2 changed from 0 to 0.08; (3) Test 2 was repeated with P_{ip} at 10 cmH_2O. A unit was classified as CO_2-sensitive or non-CO_2-sensitive based on the results of a t-test comparing the mean static discharge frequency at 0 F_ICO_2 with the static discharge frequency at the

higher level of CO_2.

RESULTS

Mechanoreceptors

A total of 247 mechanoreceptors was found in 15 bullfrogs, and 55 of these were studied in detail. Punctate stimulation with a cotton swab assured that each receptor was located within the lung (fig. 2).

1. Stretch sensitivity. Two kinds of receptors were found which differed in their response to inflation of the lung. Of the 55 receptors studied, 39 adapted slowly to inflation, and 16 adapted rapidly.

The rapidly-adapting receptors responded to inflation of the lung with a burst of activity at the onset of inflation (fig. 3A). The discharge frequency then quickly decreased (with inflation maintained) to a level approximating that before inflation. When the lung was suddenly deflated, these receptors responded with another short burst of activity.

The slowly-adapting receptors usually responded to lung inflation by an increased discharge frequency, with a dynamic overshoot at the beginnning of inflation, which decreased to a plateau as inflation was maintained (fig. 3B). Upon deflation, these receptors exhibited an undershoot in the form of a brief cessation of discharge which then gradually returned to its previous level.

2. CO_2 sensitivity. Mechanoreceptors were classified as CO_2-sensitive if they changed their discharge frequency when F_ICO_2 was changed from 0 to 0.04 or 0.08 while P_{ip} was constant. Based upon this criterion, 33 slowly-adapting receptors and fifteen rapidly-adapting receptors were sensitive to CO_2. The response of both kinds of receptors to increasing intrapulmonary CO_2 concentration (fig. 4) was a decreased discharge frequency. The rapidly-

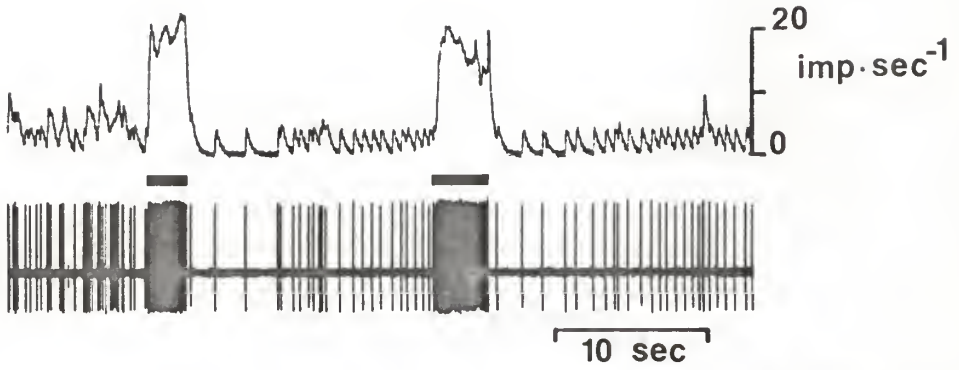

Figure 2. Response of one slowly-adapting intrapulmonary receptor to punctate stimulation of the lung with a cotton swab. Upper trace, instantaneous discharge frequency; lower trace, nerve impulses. Horizontal bars between traces indicate approximate time during which stimulus was applied.

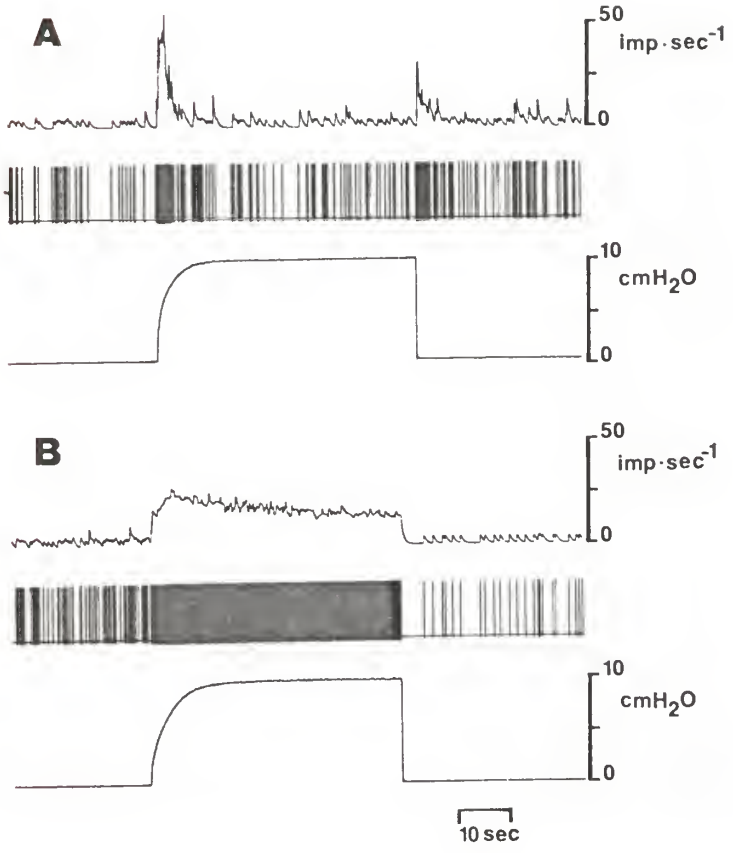

Figure 3. Response of rapidly-adapting (A) and slowly-adapting (B) mechanoreceptors to inflation and deflation of the lung. In both records: upper trace, instantaneous discharge frequency; middle trace, normalized impulses; lower trace, P_{ip}. F_ICO_2 was constant at 0.04 in both records.

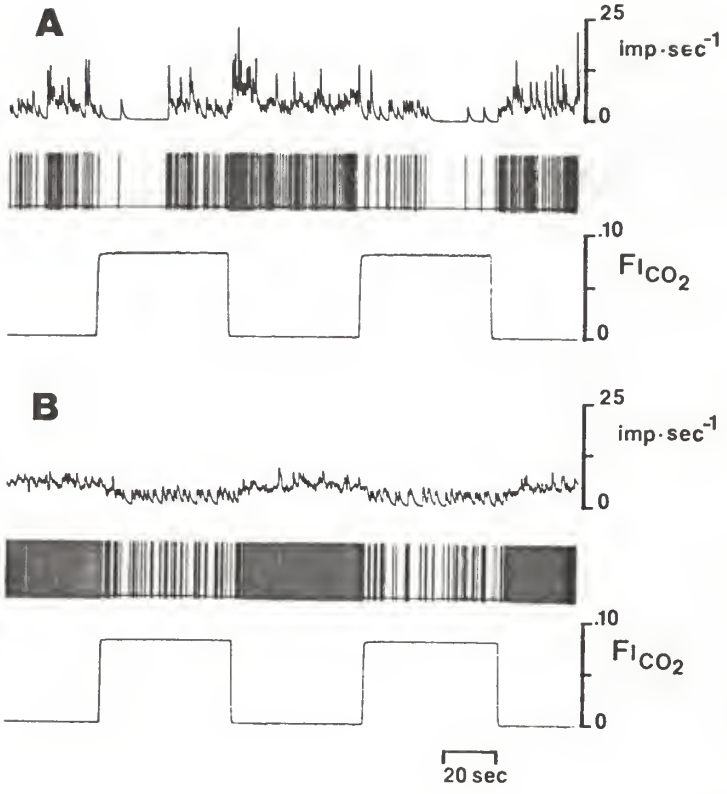

Figure 4. Response of rapidly-adapting (A) and slowly-adapting (B) mechanoreceptors to changes in intrapulmonary CO_2 concentration in the ventilating gas at constant lung inflation. In both records: upper trace, instantaneous discharge frequency; middle trace, normalized impulses; lower trace, F_ICO_2. P_{ip} is 1.0 cmH_2O in both records.

adapting receptors (fig. 4A) tended to respond more irregularly than the slowly-adapting receptors (fig. 4B).

Not all of the receptors classified as CO_2-sensitive demonstrated this sensitivity in all three of the tests. Table 1 shows the distribution of the receptors according to their response to tests (1), (2), and (3). Aside from that group of 17 receptors which responded to all three tests, two other large groups were found. One group (10 receptors) responded only to those tests in which CO_2 was elevated to 0.08. Another large group (14 receptors) did not respond to CO_2 unless P_{ip} was high. Of the remaining receptors, seven did not respond to CO_2 and seven responded to other combinations of the three tests. These results demonstrate the wide variability of these mechanoreceptors in their response to CO_2 and suggest possible interaction between the two stimuli, CO_2 and stretch.

A plot of the average discharge frequency of each of the receptors classified as CO_2-sensitive (fig. 5) clearly demonstrates that the discharge frequency of all of these receptors decreased as intrapulmonary CO_2 concentration increased. In figure 5, the rapidly-adapting and slowly-adapting receptors have been separated and their response to CO_2 is shown at two levels of P_{ip} to illustrate differences in CO_2 sensitivity between receptor types and also to indicate the effect of P_{ip} on the CO_2 sensitivity. The mean decrease in discharge frequency when F_ICO_2 was increased from 0 to 0.08 was 1.0 imp$\cdot$sec^{-1} $\pm$0.9 (SD) at low P_{ip} and 2.0 imp$\cdot$sec^{-1} $\pm$ 0.9 at high P_{ip} for slowly-adapting receptors; it was 1.7 imp$\cdot$sec^{-1} $\pm$1.3 and 3.4 imp$\cdot$sec^{-1} $\pm$1.9, respectively for the rapidly-adapting receptors. Thus, inflating the lung to 10 cmH_2O enhanced the sensitivity of these receptors to CO_2 such that the change in discharge frequency due to increasing F_ICO_2 doubled when the lung was inflated. The fact that a large group of

Table 1. Distribution of the responses of mechanoreceptors according to the various CO_2-sensitivity tests:

No. of Receptors	Test (1) P_{ip} = 1 cmH_2O F_{ICO_2} = 0-.04	Test (2) P_{ip} = 1cmH_2O F_{ICO_2} = 0-.08	Test (3) P_{ip} = 10cmH_2O F_{ICO_2} = 0-.08
17	+	+	+
10	0	+	+
14	0	0	+
7	0	0	0
2	+	0	+
2	+	+	0
3	0	+	0

+ = Significant difference in discharge frequency between high and low intrapulmonary CO_2 concentrations ($P<.05$).

0 = No significant difference in discharge frequency between high and low intrapulmonary CO_2 concentration.

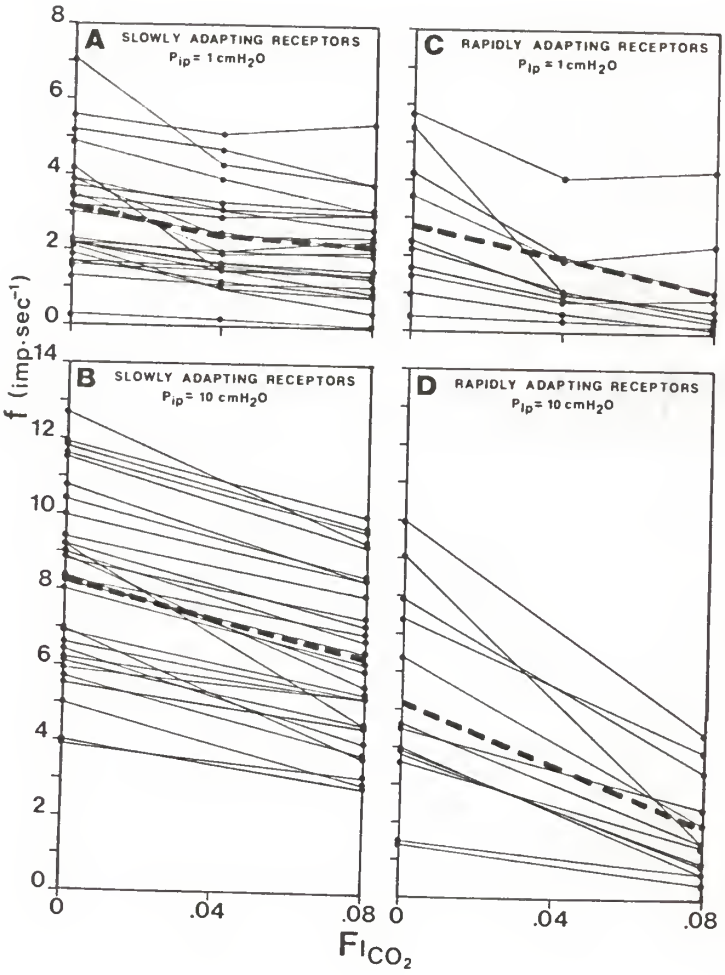

Figure 5. Static sensitivity of mechanoreceptors to various intrapulmonary CO_2 concentrations at low and high P_{ip}. Heavy dashed lines indicate the mean static CO_2-sensitivity of all receptors in each plot.

receptors did not respond to CO_2 until the lung was inflated (table 1) also supports the idea of interaction between CO_2 and stretch. It should be noted, however, that the decrease in discharge frequency, when represented as a percentage of the discharge frequency at 0 F_ICO_2, did not change when the lung was inflated. For the slowly-adapting receptors, the percent decrease was 32% $\pm$ 20 (SD) at low P_{ip} and 25% $\pm$ 10 at high P_{ip}. For the rapidly-adapting receptors, it was 64% $\pm$ 23 at low P_{ip} and 65% $\pm$ 12 at high P_{ip}. When compared by a t-test, no significant difference between high and low P_{ip} was found in these percentage changes for either kind of receptor.

CO_2 Receptors

No CO_2 receptors without stretch sensitivity, like those in the lungs of birds and reptiles, were found in the bullfrog.

DISCUSSION

CO_2 Receptors

One purpose of this study was to determine if CO_2 receptors exist in the lungs of the bullfrog. Failure to find this kind of receptor in the lungs of the bullfrog could have two possible explanations: (1) this kind of receptor does not exist in the bullfrog; or (2) the techniques used in searching for these receptors were not appropriate. Although the existence of CO_2 receptors in this animal cannot be conclusively ruled out, the methods and techniques used in searching for these receptors were identical to those successfully used on other animals. In six of the bullfrogs, the vagus was completely dissected; so it is not likely that these receptors were missed because they lie grouped in small bundles within the vagus.

CO_2-Sensitive Mechanoreceptors

Several investigations into the effect of CO_2 upon the activity of pulmonary stretch receptors have been conducted on mammals (Mustafa and Purves, 1972; Schoener and Frankel, 1972; Sant'Ambrogio, et al., 1974; Sampson and Vidruk, 1975; Bartlett and Sant'Ambrogio, 1976; Kunz, et al., 1976) and reptiles (Milsom and Jones, 1976; Fedde, et al., 1977). Therefore, it seems appropriate to compare the results of these studies in higher vertebrate classes with those found in the bullfrog.

1. Slowly-adapting pulmonary stretch receptors. The discharge frequency of mammalian slowly-adapting pulmonary stretch receptors decreases by 20% to 30% when alveolar PCO_2 (P_ACO_2) is elevated from about 20 torr to 60 torr (Mustafa and Purves, 1972; Schoener and Frankel, 1972; Sant'Ambrogio et al., 1974; Kunz, et al., 1976). Recently, it has been shown that the sensitivity to CO_2 of these receptors is even greater at alveolar PCO_2 levels below 20 torr and that the total decrease in discharge frequency when P_ACO_2 is increased from 2 torr to 60 torr is 50% or more (H. Coleridge, J. Coleridge and R. Banzett, personal communication). Fedde, et al., (1977) and Milsom and Jones (1976) report a similar sensitivity to CO_2 of reptilian slowly-adapting pulmonary stretch receptors. In the bullfrog, this kind of receptor likewise decreased its discharge frequency as P_ACO_2 is increased. However, the overall sensitivity of receptors to CO_2 in the bullfrog appears less than that of mammals and reptiles. The discharge frequency decreased by only 20% to 30% between 0 and 0.08 F_ICO_2 (approximately 0 torr and 60 torr P_ACO_2 respectively) in the bullfrog.

2. Rapidly-adapting pulmonary stretch receptors. Rapidly-adapting pulmonary stretch receptors in mammals exhibit no sensitivity to P_ACO_2

at or above normal physiological levels (Sampson and Vidruk, 1975). At low levels of P_ACO_2, however, discharge frequency has been observed to increase in the dog (H. Coleridge, J. Coleridge and R. Banzett, personal communication). These receptors apparently do not contribute to the CO_2-induced reflex hyperpnea. Rapidly-adapting stretch receptors in the bullfrog appear more sensitive to CO_2 than the slowly-adapting pulmonary stretch receptors throughout the range of 0 to 60 torr P_ACO_2. Thus, rapidly-adapting pulmonary stretch receptors may play a more important role in sensing alveolar PCO_2 levels in the bullfrog than they do in mammals.

3. Interaction between inflation and CO_2. Mustafa and Purves (1972) and Bartlett and Sant'Ambrogio (1976) report that the CO_2-sensitivity of pulmonary stretch receptors in mammals is diminished with increasing transpulmonary pressure. Their data are expressed as percent changes in average frequency from control. If the data found in this study are normalized in this manner, no difference is found in percent change in discharge frequency between high and low P_{ip} due to CO_2, and thus no apparent interaction between these stimuli. However, if CO_2-sensitivity is defined as $\Delta f/\Delta F_ICO_2$ (where Δf represents the change in discharge frequency and ΔF_ICO_2 represents the change in F_ICO_2), the percent change in discharge frequency does not adequately represent a change in CO_2-sensitivity. For example, if the discharge frequency of a receptor at 1 cmH_2O P_{ip} and F_ICO_2=0 is 4.0 imp$\cdot$sec^{-1} and this frequency decreases to 2.0 imp$\cdot$sec^{-1} when F_ICO_2 is elevated to 0.08, then the CO_2-sensitivity of this receptor could be expressed as 2.0 imp$\cdot$sec^{-1}/0.08 F_ICO_2 or, if expressed in percent change, as a 50% decrease in discharge frequency from control. Now if P_{ip} is elevated to 10 cmH_2O at F_ICO_2=0 and discharge frequency increases, due to the higher P_{ip}, to 8.0 imp$\cdot$sec^{-1} and this

frequency decreases to 4.0 imp·sec^{-1} when F_ICO_2 is elevated to 0.08 the CO_2-sensitivity becomes 4.0 imp·sec^{-1}/0.08 F_ICO_2, which is twice the value for CO_2-sensitivity found at low P_{ip}, but when expressed as a percent change it remains a 50% decrease in mean discharge frequency. Thus, caution must be exercised in comparing the CO_2-sensitivity of these receptors, between high and low P_{ip}, when expressed in percent changes from control. Therefore, the actual changes in discharge frequency (expressed in imp·sec^{-1}) were used in this study to determine the presence of interaction between the two stimuli, CO_2 and stretch. The results indicate that the CO_2-sensitivity of both slowly-adapting and rapidly-adapting pulmonary mechanoreceptors is enhanced when P_{ip} is high. This interaction appears to be directly opposite to the interaction of these stimuli in mammals (Mustafa and Purves, 1972; Bartlett and Sant'Ambrogio, 1976) and reptiles (Fedde, et al., 1977).

Smyth (1939) showed that reflex hyperpnea occurs in frogs when they are placed in an atmosphere containing as little as 2% CO_2 and that skin receptors, receptor organs in the palate, and the carotid gland do not initiate this response. The CO_2-sensitive pulmonary stretch receptors may be responsible for initiating this reflex. A similar role for CO_2-sensitive mammalian pulmonary stretch receptors has been suggested (Burger, 1968; Bartoli, et al., 1974; Bradley, et al., 1976).

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APPENDIX

Mean discharge frequency of each receptor at various CO_2 concentrations and intrapulmonary pressures. * Indicates significant difference in discharge frequency when compared to the discharge frequency at $F_ICO_2=0$ using t-test ($P<.05$).

Animal No.	Unit No.	Type of receptor	F_ICO_2	$\bar{f}$ (imp·sec^{-1}) $P_{ip}=1cmH_2O$	$\bar{f}$ (imp·sec^{-1}) $P_{ip}=10cmH_2O$
8	1	Slowly adapting	0.00	2.1	7.0
			0.04	1.0*	---
			0.08	0.8*	3.6*
	2	Rapidly adapting	0.00	1.8	4.5
			0.04	1.1	---
			0.08	1.5	2.4*
11	1	Rapidly adapting	0.00	2.2	2.7
			0.04	1.1	---
			0.08	0.4*	1.5
	2	Rapidly adapting	0.00	1.1	3.6
			0.04	0.8	---
			0.08	0.5	1.4*
	3	Slowly adapting	0.00	6.0	9.2
			0.04	6.3	---
			0.08	5.4	7.1*
	4	Slowly adapting	0.00	2.4	4.6
			0.04	1.7	---
			0.08	2.4	4.3
	5	Slowly adapting	0.00	2.4	5.7
			0.04	1.9*	---
			0.08	2.0*	3.7*
	6	Slowly adapting	0.00	2.8	6.7
			0.04	2.6	---
			0.08	2.8	6.7
	7	Slowly adapting	0.00	1.9	6.6
			0.04	1.9	---
			0.08	1.8	5.2*
	8	Rapidly adapting	0.00	5.8	7.9
			0.04	4.0	---
			0.08	4.3*	3.4*
	9	Slowly adapting	0.00	0.8	11.9
			0.04	1.1	---
			0.08	0.8	10.0*

APPENDIX (cont'd)

Animal No.	Unit No.	Type of Receptor	F_ICO_2	$\bar{f}$ (imp·sec^{-1}) P_{ip}=1cmH_2O	$\bar{f}$ (imp·sec^{-1}) P_{ip}=10cmH_2O
11	10	Rapidly adapting	0.00	8.8	10.0
			0.04	6.0	---
			0.08	8.5	4.4*
	11	Rapidly adapting	0.00	1.7	3.0
			0.04	0.9*	---
			0.08	0.3*	1.6
	12	Slowly adapting	0.00	2.6	3.9
			0.04	2.3	---
			0.08	2.5	3.1*
14	1	Rapidly adapting	0.00	4.4	9.0
			0.04	3.0	---
			0.08	3.9	10.0
	2	Slowly adapting	0.00	3.8	5.9
			0.04	3.6	---
			0.08	3.1	5.2*
	3	Slowly adapting	0.00	2.2	6.2
			0.04	2.0	---
			0.08	2.0	5.2*
	4	Slowly adapting	0.00	3.5	5.5
			0.04	3.1	---
			0.08	3.0*	4.4*
	5	Rapidly adapting	0.00	3.6	7.4
			0.04	1.9*	---
			0.08	2.3*	3.9*
	6	Rapidly adapting	0.00	0.9	4.6
			0.04	0.7	---
			0.08	0.7	1.5*
	7	Rapidly adapting	0.00	1.1	1.4
			0.04	0.5	---
			0.08	0.1*	0.4*
	9	Slowly adapting	0.00	1.9	4.0
			0.04	1.0*	---
			0.08	0.4*	2.8*
	11	Slowly adapting	0.00	2.3	8.4
			0.04	1.7	---
			0.08	2.9	5.8*

APPENDIX (cont'd)

Animal No.	Unit No.	Type of Receptor	F_ICO_2	$\bar{f}$ (imp.sec^{-1}) P_{ip}=1cmH_2O	$\bar{f}$ (imp.sec^{-1}) P_{ip}=10cmH_2O
14	12	Slowly adapting	0.00	5.6	11.8
			0.04	5.1*	---
			0.08	5.4	9.6*
	13	Slowly adapting	0.00	2.7	6.7
			0.04	2.5	---
			0.08	2.7	6.2
16	1	Slowly adapting	0.00	0.3	8.0
			0.04	0.3	---
			0.08	0.3	7.5
17	4	Slowly adapting	0.00	4.0	8.9
			0.04	3.1*	---
			0.08	2.6*	5.5*
	5	Slowly adapting	0.00	1.0	9.0
			0.04	0.7	---
			0.08	0.9	6.7*
	6	Slowly adapting	0.00	4.0	10.0
			0.04	2.4*	---
			0.08	2.4*	8.3*
	7	Rapidly adapting	0.00	0.4	4.0
			0.04	0.3	---
			0.08	0.2*	0.7*
	8	Slowly adapting	0.00	1.7	1.1
			0.04	1.2	---
			0.08	0.8*	0.9
	9	Slowly adapting	0.00	2.7	4.3
			0.04	2.6	---
			0.08	2.8	4.1
18	1	Rapidly adapting	0.00	2.4	6.4
			0.04	1.0*	---
			0.08	0.6*	2.0*
19	1	Slowly adapting	0.00	6.1	7.7
			0.04	5.7	---
			0.08	6.6	7.8
	2	Slowly adapting	0.00	2.2	6.1
			0.04	2.0	---
			0.08	1.9*	4.5*
	4	Slowly adapting	0.00	1.6	6.9
			0.04	1.5	---
			0.08	1.4*	5.3*

APPENDIX (cont'd)

Animal No.	Unit No.	Type of Receptor	F_ICO_2	$\bar{f}$ (imp.sec^{-1}) P_{ip}=1cmH_2O	$\bar{f}$ (imp.sec^{-1}) P_{ip}=10cmH_2O
20	1	Slowly adapting	0.00	7.1	9.2
			0.04	4.3*	---
			0.08	3.8*	4.5*
21	2	Slowly adapting	0.00	5.2	10.4
			0.04	4.7	---
			0.08	3.8*	8.4*
	3	Slowly adapting	0.00	1.3	5.6
			0.04	1.1	---
			0.08	1.1*	5.1
	4	Slowly adapting	0.00	1.7	8.0
			0.04	1.6	---
			0.08	1.2*	6.1*
	5	Slowly adapting	0.00	2.2	8.8
			0.04	1.7*	---
			0.08	1.5*	7.3*
	6	Slowly adapting	0.00	0.3	8.3
			0.04	0.2	---
			0.08	0.3	6.9*
	7	Slowly adapting	0.00	3.3	6.4
			0.04	2.9	---
			0.08	3.0*	4.0*
	8	Rapidly adapting	0.00	1.5	3.9
			0.04	0.8*	---
			0.08	0.9	0.9*
22	1	Slowly adapting	0.00	3.7	10.8
			0.04	3.3	---
			0.08	3.1*	8.3*
	2	Slowly adapting	0.00	3.0	11.6
			0.04	2.6*	---
			0.08	2.1*	9.6*
	3	Rapidly adapting	0.00	4.3	3.8
			0.04	2.0*	---
			0.08	1.1*	1.0*
	4	Rapidly adapting	0.00	5.4	9.1
			0.04	1.1*	---
			0.08	0.6*	1.5*

APPENDIX (cont'd)

Animal No.	Unit No.	Type of Receptor	$F_I CO_2$	$\bar{f}$ (imp·sec^{-1}) P_{ip}=1cmH_2O	$\bar{f}$ (imp·sec^{-1}) P_{ip}=10cmH_2O
23	1	Slowly adapting	0.00	2.2	8.2
			0.04	1.4*	---
			0.08	1.4*	6.4*
	2	Slowly adapting	0.00	2.2	12.7
			0.04	1.7*	---
			0.08	1.4*	9.3*
	3	Rapidly adapting	0.00	0.2	1.5
			0.04	0.2	---
			0.08	0.4	0.7*
24	1	Slowly adapting	0.00	0.3	11.5
			0.04	0.2*	---
			0.08	0.0*	9.2*
26	1	Slowly adapting	0.00	4.2	10.6
			0.04	1.4*	---
			0.08	0.9*	6.5
27	1	Slowly adapting	0.00	4.9	9.4
			0.04	3.9*	---
			0.08	3.1*	7.9*
29	1	Slowly adapting	0.00	3.4	5.0
			0.04	2.0*	---
			0.08	2.3*	2.9*

INTRAPULMONARY RECEPTORS IN THE BULLFROG: SENSITIVITY TO CO_2

by

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AN ABSTRACT OF A MASTER'S THESIS

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ABSTRACT

The effect of CO_2 upon the discharge frequency of intrapulmonary receptors was studied in 15 bullfrogs (Rana catesbeiana). The purposes of the study were (i) to determine if receptors whose adequate stimulus is CO_2 are present in the frog lung and (ii) to determine if CO_2 alters the discharge frequency of intrapulmonary mechanoreceptors in the frog. The animals were either anesthetized or decerebrated and a unidirectional ventilation system was used to provide a constant flow of gas through the lung. Specialized valves in the gas stream allowed independent control of intrapulmonary CO_2 concentration (FCO_2) and intrapulmonary pressure (P_{ip}). Single-unit vagal activity, FCO_2, and P_{ip} were recorded on magnetic tape for analysis.

Of 247 mechanoreceptors found 55 were studied in detail. Of these 55 receptors, 39 exhibited a slowly adapting response to inflation of the lung and 16 exhibited a rapidly adapting response. Most of the receptors (48) decreased their discharge frequency when FCO_2 was increased. This response to CO_2 was variable and in some receptors did not appear until FCO_2 was elevated above 0.04. Increasing P_{ip} to 10 cmH_2O had the effect of enhancing the response of the receptors to CO_2, indicating that an interaction exists between the stimuli, CO_2 and stretch.

No receptors were found whose adequate stimulus was CO_2, as have been found in the lungs of birds and reptiles.

The CO_2 sensitive mechanoreceptors found in the bullfrog are qualitatively similar to those reported in the lungs of mammals and reptiles and may play an important role in the control of breathing.